

# Blood Donor Screening for Chagas Disease

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# Outline

- Transfusion transmitted cases
- 2002 Initial Seroprevalence study results
- US transplant transmitted cases
- 2006 Ortho Chagas Prevalence Protocol
- 2006 Prevalence study results
- Donor follow up protocol

# *US/Canadian Transfusion Cases*

1987: California - Mexican donor

1989: New York City - Bolivian donor  
Manitoba - Paraguayan donor

1993: Houston - unknown donor

1999: Miami - Chilean donor\*

2000: Manitoba - German/Paraguayan donor  
(same Mennonite community as above)

2002: Rhode Island – Bolivian donor

\*Leiby et al, NEJM, 1999; 341(16):1237-1239

# Transfusion Cases

*Transfusion; 2007; 47(3) 540-544*

## ● Seventh case reported 3/07

- Rhode Island case
- 3 ½ yo with neuroblastoma
- Received 78 blood products
- Blood smear showed parasites
- Implicated first time donor emigrated from Bolivia 17 years earlier w/o return to Chagas endemic area
- Donor IFA positive; PCR negative

# *T. cruzi* Seroprevalence Study in Los Angeles and Miami

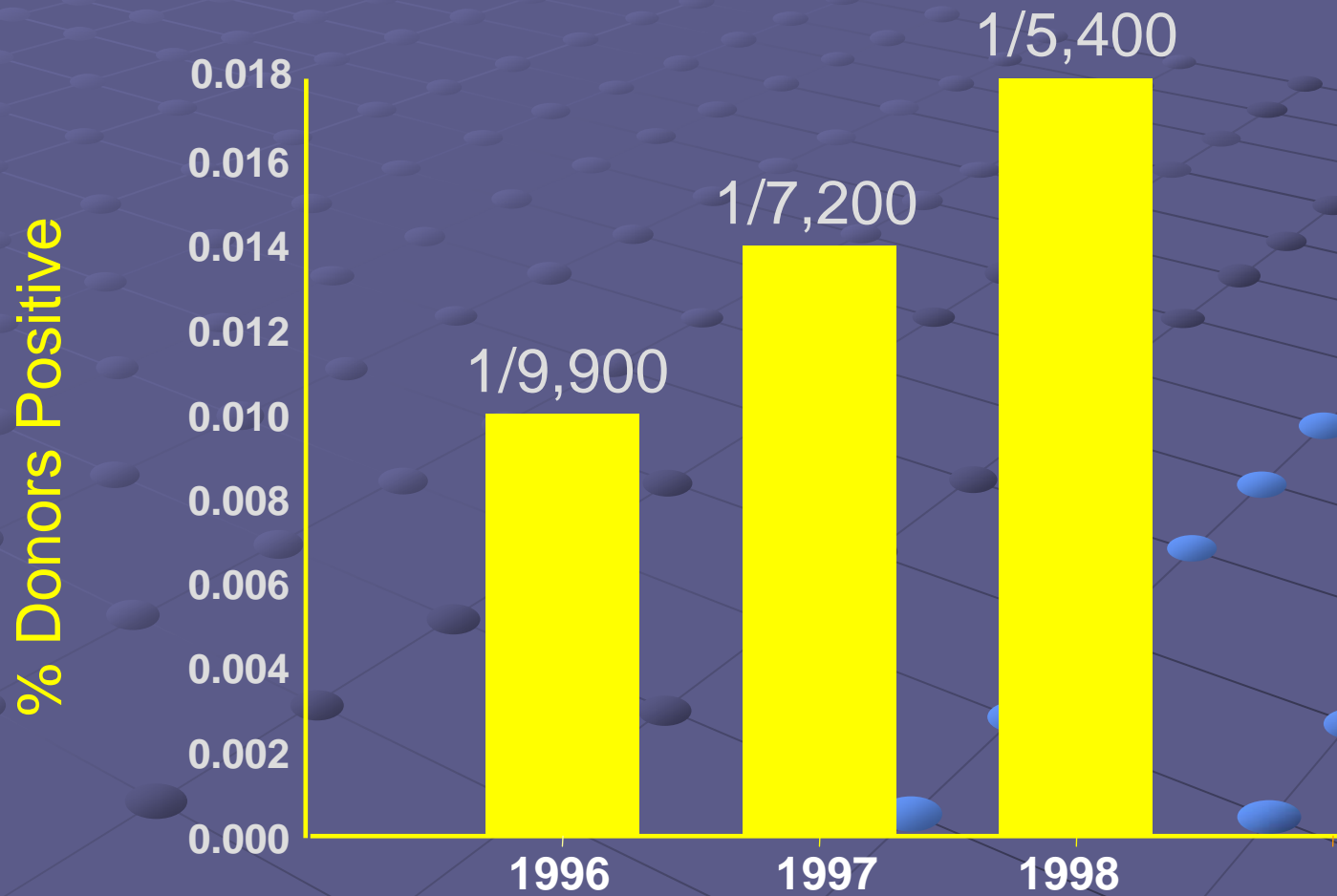
*Transfusion; 2002; 42(5) 549-555*

- Conducted in LA 5/1994 to 9/1998 and Miami 8/1994 to 1/1998
- Donations from donors who answered 'yes' to questions "Were you born in Mexico, Central America or South America?" or "Have you ever spent more than 6 months in any of those places?" were tested for antibody to *T. cruzi*

# *T. cruzi* Seroprevalence Study in Los Angeles and Miami

- LA over 1.1 million donations screened with 7.1% responding yes with 77,967 donors tested
- Miami 181,139 screened with 14.3% responding yes with 25,352 donors tested
- Overall seropositive rate for LA was 1:7500 and Miami 1:9000

# *LA Seroprevalence: 1996-98*





# US Transplant Cases

MMWR; 2001; 51(10):210-2

- Three cases from a single donor
  - 37 yo female rec'd kidney and pancreas
    - febrile with trypomastigotes on blood smear
  - Died of acute Chagas myocarditis (2 weeks post treatment)
  - 32 yo female rec'd liver
    - Smear positive; died unrelated causes
  - 69 yo female rec'd kidney
    - Smear positive; completed nifurtimox treatment; no recurrence of *T. cruzi* infection
  - Donor from Central America, presumed infected with *T. cruzi* but never tested



# US Transplant Cases

MMWR; 2006; 55(29):798-800

## ● Case 1: 2/17/06

- 64 yo male heart transplant recipient (12/05); no history infection/travel
  - Seronegative post transplant (IFA), PCR and culture pos, trypomastigotes on blood smear
  - Native heart and all blood received negative
  - Nifurtimox cleared parasitemia
- **Organ donor; US born young male, traveled once to Mexico (2-3 months Guadalajara)**
  - Liver and 2 kidney recipients IFA and PCR neg
  - Serum IFA borderline +; **RIPA positive**
  - “Nests” of amastigotes seen in endomyocardium
  - All blood to organ donor negative

# US Transplant Cases

MMWR; 2006; 55(29):798-800

## ● Case 2: 2/24/06

- 73 yo male heart transplant recipient; no history infection/travel
  - Seronegative post transplant (IFA), PCR (plasma and CSF), culture pos, trypomastigotes on blood smear
  - Native heart and all blood received negative
  - Nifurtimox cleared parasitemia
- **Organ donor; El Salvadoran male immigrant**
  - Liver and 2 kidney recipients IFA and PCR neg
  - Serum IFA neg; **RIPA positive**
  - All blood to organ donor negative
    - *1 FFP not tested; parasite doesn't survive freezing*

# Chagas Transplant Cases

- CDC acknowledged the prevalence of infection with *T.cruzi* varies by region but is probably higher than once thought
- Areas such as LA county where a high proportion of donors have emigrated from Chagas endemic countries is cause for concern

# Chagas Protocol

- FDA request of Ortho to expand clinical studies to include areas where *T. cruzi* antibody prevalence previously documented
  - Pivotal Clinical Trial yield 0 confirmed positive (of 40,665 tested)
  - 100,000 donations to define the study
  - SoCal, NoCal and AZ (West ARC Division)
    - FDA requirements for donor informed consent
      - Use of an information sheet with signature on BDR acknowledging receipt not allowed
      - Specific signature **and date** required on info sheet
    - Due to these requirements, other blood centers declined

# Chagas Protocol

- All IR donors deferred ( $S/CO > 0.75$ ) and cellular components discarded; plasma sent to Red Cross
  - All RR donors or IR who are RIPA ind/pos enrolled in follow up study
- Lookback following HCV model
  - Prior in-date components quarantined/retrieved and recipients of prior components from confirmed positive donors notified and testing requested as long as electronic records exist (HCV model)
- Confirmatory/counseling/reentry
  - No gold standard; no single test is adequately sensitive, not even RIPA
    - Will likely require several tests and validated algorithm; Wendel AABB; 2005
    - However, for the purposes of this study/implementation, RIPA would be used



# Chagas Protocol

- Additional testing

- All IRs sample sent from BSL to Ortho Rochester for RIPA
  - *Leishmania* Ab testing (cross reactivity) if RIPA neg/ind
- Retrieved frozen plasma
  - RIPA at the Red Cross (Holland Labs; David Leiby)
- Follow up
  - Sample sent from region to Blood Systems for ELISA
    - RR sent to Ortho for RIPA
  - Additional sample (David Leiby)
    - RIPA
    - PCR
    - Hemoculture
  - Donor Risk Questionnaire

**Chagas ELISA Initial and/or Repeat Reactive**

**Perform RIPA**

**Pos**

**Donor  
Indefinitely  
Deferred**

**Ind**

**Donor  
Deferred**

**Neg**

**Donor  
Deferred**

**ELISA RNR**

**Donor  
Reinstated**

**ELISA RR**

**Donor Follow-Up ELISA and  
RIPA**

**ELISA RR/RIPA  
Ind/ Positive**

**All other  
test results negative**

**Donor  
Deferred  
Indefinitely**

**Donor may  
be eligible for  
reentry after  
a licensed test  
is available**



# Chagas Early Study Results 8/28-12/22/06

	<b>All sites</b>	<b>SoCal</b>	<b>Arizona</b>	<b>NoCal</b>
<b>Total Attempted Donors</b>	<b>145,331</b>	<b>97,764</b>	<b>19,926</b>	<b>27,641</b>
<b>Total Tested</b>	<b>120,340</b>	<b>78,827</b>	<b>17,851</b>	<b>23,662</b>
<b>Total RR</b>	<b>47 (1:3092)</b>	<b>41 (1:2384)</b>	<b>1</b>	<b>5 (1:5528)</b>
<b>Total (%) Refusals</b>	<b>24,991 (17.2%)</b>	<b>18,937 (19.3%)</b>	<b>2075 (10.4%)</b>	<b>3979 (14.4%)</b>

24,991 refusals/detection rate of 1:3092= 8.1 undetected donors!

# Blood Donor Screening for Chagas Disease in US-2006-2007

MMWR; 2007; 56(07):141-143

- 148,969 blood samples collected 8-2006 through 1-2007
- 63 samples from 61 donors RR for *T. cruzi* abs
- 32 donations confirmed positive for *T. cruzi* abs (1:4655 donations)

# Blood Donor Screening for Chagas Disease in US-2006-2007

MMWR; 2007; 56(07):141-143

## ● 61 donors:

- 66% male
- 17-84 yo (mean-47; median-50)

## ● 63 RR samples:

- 50 collected in LA (79%; 1:1993 donations)
- 9 collected in Oakland (14%; 1:3258 donations)
- 4 collected in Tucson (6%; 1:5995 donations)

# Blood Donor Screening for Chagas Disease in US-2006-2007

MMWR; 2007; 56(07):141-143

- 56 donors were allogeneic; 5 autologous
- 33% were first time donors
- 67% were repeat donors
- Important implications for recruitment in high prevalence areas

# Chagas Early Study Results 8/28-12/22/06

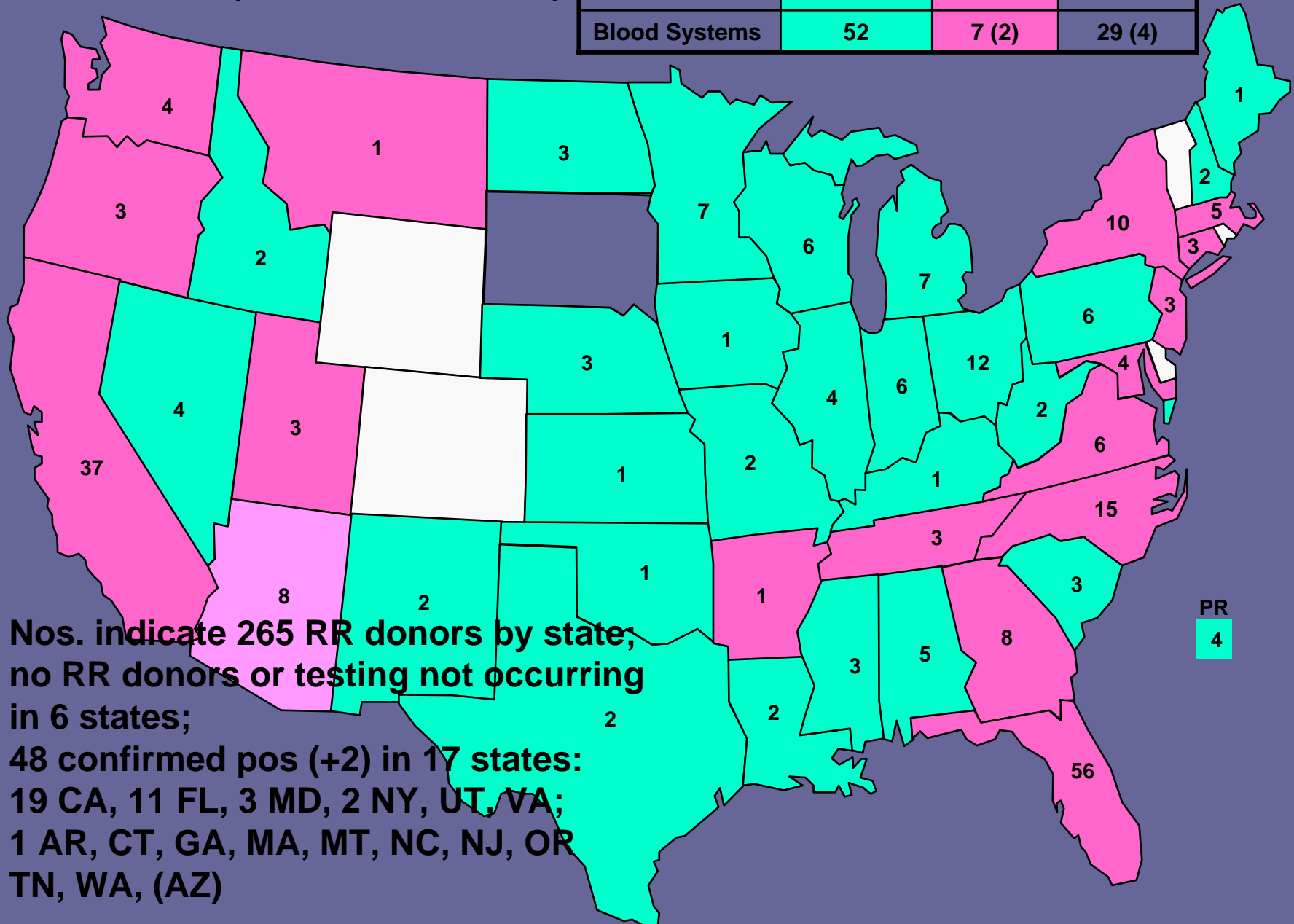
- On December 13, 2006 based in part on this preliminary data the FDA licensed the Ortho *T.cruzi* ELIZA Test System to screen blood donors in the U.S.
- The test is NOT mandatory
- No confirmatory test has been approved for blood donor screening
- No reentry protocol exists at this time

# Test Performance

- ARC Clinical trial (8/28/06-1/28/07)
  - PPV = 32 RIPA pos/63 RR = 51%
  - Prevalence = 32/148,969 = 1:4655
  - Specificity = 148,906 test neg/148,906+31 false pos = 99.979%
- Nationwide screening (1/29/07-4/17/07)
  - PPV = 50 RIPA pos/224 RR RIPA tested = 22%
    - 30 of 50 (60%) RIPA pos from 2 states (CA, FL)
  - RR rate = 265 RRs (213 ARC + 52 BSL)/1,757,800 donations = 0.015%
  - Projected prevalence based on 22% PPV of RIPA tested = 1:30,150
  - Specificity (ARC) first week = 124,934 test neg/124,934+28 false pos = 99.978% (6 pos)
- Overall prevalence = 1:21,100, and 27% rate of RIPA positivity

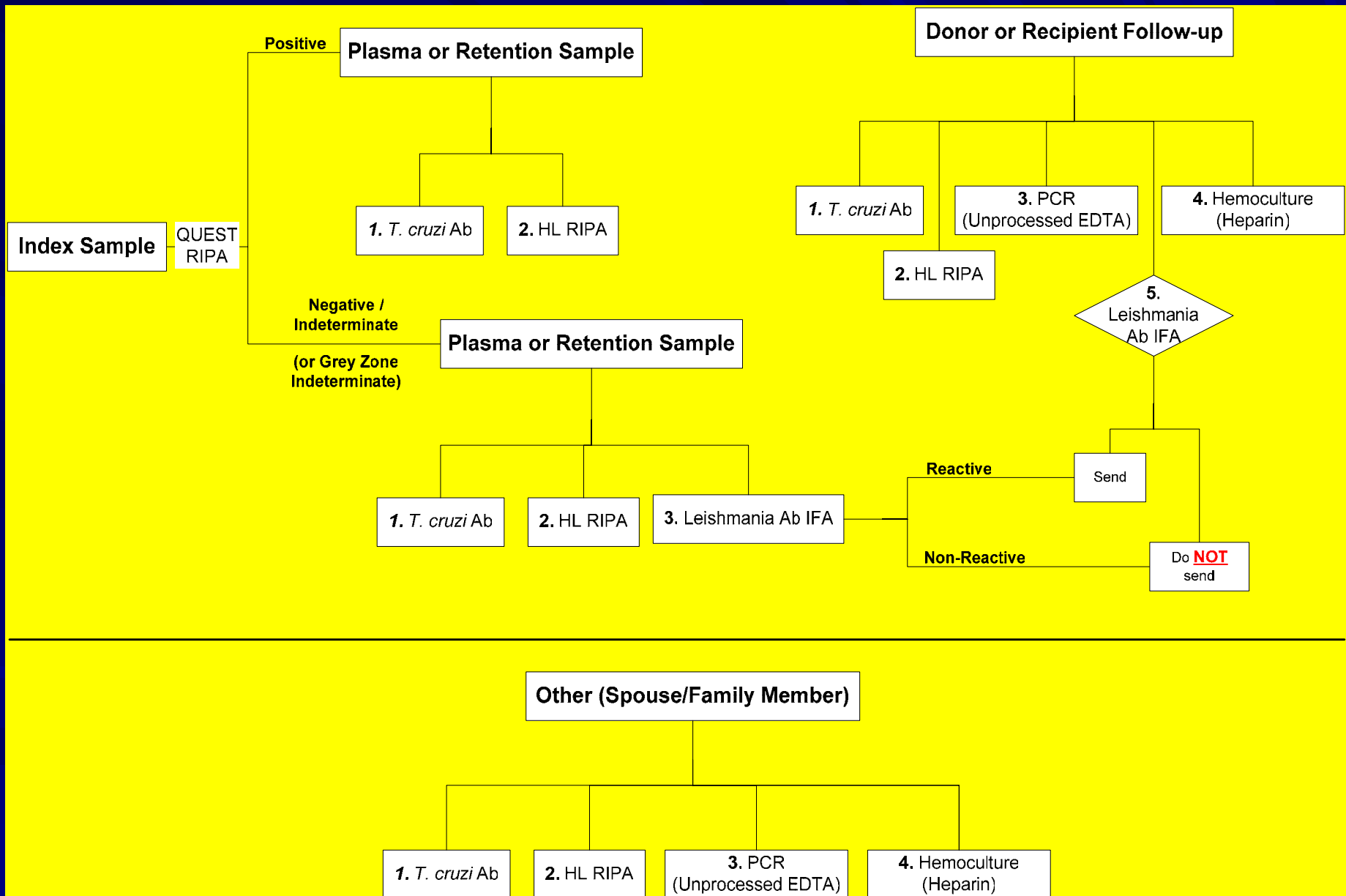
# *T. cruzi* Reactive Donors by State of Residence (01/29/07 – 04/17/07)

	Total RR Donors	RIPA Pos	RIPA Reported
ARC	213	41	191
Blood Systems	52	7 (2)	29 (4)





# IVD Testing Algorithm



# Donor Demographics

- Total 328 RR donors (IND, IVD)
  - 82 RIPA pos
    - 40 FT, 42 RPT
    - 53 males, 29 females
    - 76 allo, 3 platelet pheresis, 2 auto, 1 directed
    - Countries represented (N=33): Mexico (13), El Salvador (7), US (5), Bolivia (3), Guatemala (2), Venezuela (1), Argentina (1) Brazil (1)
    - 28/33 (85%) endemic areas

# Donor Follow-up Study

## ● Four page questionnaire:

- Place of birth
- Country of residence
- Housing
- Transfusion history
- Symptoms
- Presence of cardiac/GI diseases
- Additional samples may be drawn
- Family members may be included

# Summary

- Prevalence is 1:21,100
- 60% of cases from California and Florida
- FDA approved a single test for screening blood donors on 12/13/06
- Addressing Chagas Disease transmission is an ongoing effort by all of the major blood banking organizations in the US

# Acknowledgements

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